DuPont Haskell Global Centers
for Health and Environmental Sciences
1090 Elkton Road
Newark, DE 19711

CBIC Control Number
364858

April 28, 2015

Via Federal Express

Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Ave., NW
Washington, DC 20004

Dear 8(e) Coordinator:

Chemical Name: Dimethyl Maleate
CAS# 624-48-6

This letter is to inform you of the results of an in vitro genetic toxicity study with the above referenced test substance.

The test substance was evaluated to determine its ability to induce forward mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells in the presence and absence of Aroclor-induced rat liver S9. The test substance was evaluated in a preliminary toxicity assay at concentrations from 5.63 to 1440 µg/mL (the highest concentration evaluated approximated the 10 mM limit dose for this assay). Relative suspension growth (RSG) was 9, 8 and 16% at concentrations of 180 µg/mL (4-hour treatment with S9), 90.0 µg/mL (4-hour treatment without S9), and 22.5 µg/mL (24 hour treatment without S9), respectively. RSG was 0% at all higher concentrations. Based on the results of the preliminary toxicity assay, cultures were treated at concentrations of 11.3, 20.0, 35.6, 47.5, 63.3, 84.4, 113, 150 and 200 µg/mL (4-hour treatment with S9), 4.22, 8.45, 15.0, 26.7, 47.5, 63.3, 84.4 and 113 µg/mL (4 hour treatment without S9), and 1.06, 2.11, 4.22, 8.45, 15.0, 20.0, 26.7 and 35.6 µg/mL (24 hour treatment without S9) in the mutagenicity re-test assay. Cultures treated at concentrations of 11.3, 20.0, 47.5, 84.4 and 150 µg/mL (4-hour treatment with S9), 15.0, 26.7, 47.5 and 63.3 µg/mL (4-hour treatment without S9), and 4.22, 8.45, 15.0, 20.0 and 26.7 µg/mL (24 hour treatment without S9) exhibited 19 to 96%, 44 to 102%, and 33 to 109% RSG, respectively, and were cloned. Relative total growth of the cloned cultures ranged from 17 to 90% (4-hour treatment with S9), 24 to 99% (4 hour treatment without S9) and 22 to 92% (24-hour treatment without S9). Dose-dependent increases in induced mutant frequency, exceeding 90 mutants per 106 clonable cells, were observed under all three treatment conditions. Colony size distributions indicated the increases in mutant frequency in the test substance treated cultures were primarily due to an increase in small colonies, which is consistent with a clastogenic mechanism of action. All positive and vehicle control values were within acceptable ranges, and all criteria for a valid study were met. These results indicate the test substance was positive in the L5178Y/TK+/- Mouse Lymphoma Assay both in the presence and absence of Aroclor induced rat liver S9.

This information is submitted in accordance with current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act or, where it is not clear that reporting criteria have been met, it is submitted as a precautionary measure and because it is information in which EPA may have an interest.

Sincerely,

S. Satheesh Anand, Ph.D., DABT
Senior Research Toxicologist
SSA/MD: jhh
(302) 366-5314

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